REMARKS

Claims 2, 3, 5, 12, 14 to 22, and 42 are pending and under examination. Applicants propose to amend claim 2 to recite "at least one biopolymer" and to amend claim 42 to depend from claim 2. Both of these amendments were suggested by the Office. This amendments are supported throughout the specification and would add no new matter to the specification. Furthermore, the proposed claim amendments would raise no new issues and require no additional searching by the Examiner, and instead would place the claims into condition for allowance or at least put the claims into better condition for appeal.

Withdrawn Objections/Rejections

Applicants acknowledge the Office's withdrawal of the previous objection to claim 5 and the rejection of claims 2, 3, 5, 12, 14 to 22 and 42 for alleged double patenting.

Objection to the Claims

Claim 3 has been objected to for allegedly failing to further limit the subject matter of claim 2. In the interest of moving the present application toward allowance, applicants propose to amend the claim as suggested by the Office. Accordingly, applicants request that this amendment be entered and that the objection be reconsidered and withdrawn.

Claim 42 has been objected to for depending from canceled claim 1. In the interest of moving the present application toward allowance, applicants propose to amend this claim to depend from claim 2 rather than claim 1, as suggested by the Office. Accordingly, applicants request that this amendment be entered and that the objection be reconsidered and withdrawn.

Rejection under 35 U.S.C. 103(a)

Claims 2, 3, 5, 12, and 14 to 22 were rejected under 35 U.S.C. 103(a) as allegedly obvious over U.S. Patent 6,458,287 (Scott) in view of WO 98/30207 (Watts) and further in view of the teachings of Noble (US 4,574,152), Voser (US 3,725,400) and Chromecek (3,886,125). In maintaining the rejection, the Office Action states (at page 3):

Applicant traverses this rejection on the basis that the claims have been amended to exclude embodiments where additional complexing agents to the metal cation are present in the composition, and because the Scott reference teaches that the macromolecule complexing agents are required for the incorporation of compounds not having a tertiary structure into the polymeric microparticles. In view of these arguments, the rejection is restated as a rejection of claims 2, 3, 5, 12, 14-22 were rejected under 35 U.S.C. 103(a) as being unpatentable over Scott in view of Watts, and further in light of the teachings of Noble (U.S. 4,574,152), Voser (U.S. 3,725,400), and Chromecek (U.S. 3,886,125). In view of the restatement, Applicant's arguments are not found persuasive.

As indicated above, Applicant argues that the Scott reference indicates that the presence of a macromolecule is required for the incorporation of small-molecule drugs into the described particles. However, it is noted that the reference does not state that the macromolecules are required. Rather, the reference indicates that such small molecules "can be formed into a microsphere by incorporation or coupling of the compound to a carrier molecule that has a tertiary structure" (emphasis added). As was previously noted in the action of March 14, 2003 (page 8), the Scott reference also teaches that the metal cations are also complexing agents that are capable of interacting with therapeutic agents. Thus, those of ordinary skill in the art would have understood that the use of these agents would be an alterative to the use of the macromolecular complexing agents.

* * *

While the Scott reference teaches the additional inclusion of the macromolecule complexing agents, because the additional teachings in the art indicate that such would not be required for the incorporation of a cephalosporin into the complex, it would have been obvious to those of ordinary skill in the art to leave out such particles.

Applicants respectfully disagree and again traverse this rejection. Scott is clear as to what components are required in Scott's microspheres for sustained release of therapeutic agents. At a minimum, Scott's microspheres require a macromolecule and at least one water soluble polymer (see Scott at col. 3, lines 27 to 30 and col. 10, lines 43 to 46). According to Scott, a macromolecule is "any molecule having a tertiary and quaternary structure or capable of having a tertiary and quaternary structure." (col. 12, lines 22 to 24). Preferred macromolecules include, e.g., proteins, peptides, carbohydrates, polysaccharides and nucleic acids (col. 12, lines 24 to 30). Scott's microspheres can further include one or more complexing agents which, according to Scott, are molecules capable of interacting with a therapeutic agent to facilitate loading, retaining

and/or otherwise delaying the release of a therapeutic agent from a microsphere (col. 5, lines 8 to 18). Complexing agents include, e.g., divalent metal cations such as calcium, magnesium and zinc (col. 5, lines 26 to 37). In sum, Scott requires that the microsphere includes a macromolecule and a polymer, and optionally a complexing agent.

In essence, the Office argues that skilled practitioners would have read Scott, the primary reference, along with a number of secondary references, as somehow teaching that the macromolecule is merely an optional part of Scott's microspheres. The Office therefore proposes to modify Scott to simply leave out the macromolecule in an attempt to arrive at the present invention. Applicants do not see how this could be the case. For its part, Scott does not teach, or even suggest, that the core portions of Scott's microspheres, i.e., the macromolecule and water soluble polymer, are optional. Nor does it teach or suggest that macromolecules can be left out or swapped for another component described in Scott's specification, such as a complexing agent. To be sure, Scott suggests that other components, such as complexing agents, are optional. But Scott is clear that the solution to the problem it describes, i.e., the need for a microsphere that provides sustained release of therapeutic agents *in vivo* and *in vitro*, resides in Scott's microspheres, which include a macromolecule required for three-dimensional structure.

The Office, apparently recognizing that Scott's microspheres would need to be severely modified if used in an attempt to arrive at the present invention, points out that Scott states: "active agents can be loaded into microspheres that lack complexing agents," and opines that this suggests to skilled practitioners that unnecessary components can be omitted. Scott may very well suggest that optional components can be omitted. However, it does not suggest that the macromolecule, which is a key component of the microspheres, is optional or that it can be omitted. This becomes even more clear when one considers the sentence of Scott that immediately follows that cited by the Office. That sentence describes the alternative to loading using complexing agent, stating "[a]lternatively, the active agent can be loaded into the above-described microspheres which lack a complexing agent, e.g., the protein and/or the water soluble polymers of the invention can interact with the active agent to facilitate loading and/or modify its release from the microsphere." (col. 6, lines 48 to 53). Thus, although Scott may suggest that certain components may be left out, that suggestion clearly does not apply to the core portions of

Scott's microspheres, i.e., the macromolecule and the polymer. These are required components of Scott's microspheres.

Indeed, the Office's position that Scott could have been modified to exclude macromolecules is untenable because such a drastic modification would have rendered Scott unsatisfactory for its intended purpose, i.e., to provide microspheres capable of sustained release of therapeutic agents. Again, Soctt requires a macromolecule for the purpose of providing three dimensional structure. The Office's theory is therefore not a viable foundation upon which to base this rejection. Applicants respectfully direct the Office's attention to a particularly relevant section of the Manual of Patent Examining Procedure (MPEP), which states "[i]f proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)[.]" (MPEP §2143.01(V)). It's clear that contrary to the Office's interpretation of Scott, no skilled practitioner would have understood Scott to suggest that the macromolecules could have been left out, nor would they have been motivated or given any reason by Scott (or any other reference) to do so. Such a modification would simply have destroyed the purpose of Scott's microspheres. It also follows that no skilled practitioner would have had a reasonable expectation of success in doing so given, for example, Scotts teachings about the importance of the macromolecules to Scott's microspheres.

Turning now to the secondary references, applicants submit that none of them, i.e., Watts, Noble, Voser or Chromecek, remedy the deficiencies of Scott. Watts describes, *inter alia*, drug compositions comprising chitosan, type A cationic gelatin, and a therapeutic agent. Noble describes ternary complexes that include cephalosporin complexed with copper (II) ions and an organic nitrogen base. Voser describes isolating cephalosporin C from solutions. Chromecek describes polymer complexes that include a polymer containing aluminum zinc or zirconium metal bound in complex form. Not one of these references provides the motivation or reasoning to which the Office refers, i.e., a motivation to modify Scott to leave out a core portion of Scott's microspheres. Accordingly, applicants submit that no *prima facie* case of obviousness has been established and that the present rejection should be reconsidered and withdrawn.

Claims 2, 3, 5, 12, 14 to 22, and 42 were rejected as allegedly obvious over Scott in view of Watts and U.S. Patent No. 5,783,561 (Horwitz) and further in view of the teachings of Noble

(US 4,574,152), Voser (US 3,725,400) and Chromecek (3,886,125). Applicants traverse this rejection.

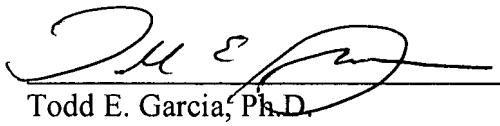
The deficiencies of Scott, Watts, Noble, Voser and Chromecek were discussed above in detail. Horwitz does not remedy the deficiencies of these references. Horwitz describes, *inter alia*, treating gram positive bacterial infections using bactericidal/permeability-increasing (BPI) protein products. Horwitz would not have provided skilled practitioners with any motivation or reason to modify Scott in the way the Office proposes, and apparently Horwitz is not relied upon by the Office for such a teaching. Thus, the combination of Scott, Watts, Horwitz, Noble, Voser and Chromecek do not support a *prima facie* case of obviousness and the rejection should be withdrawn.

CONCLUSION

Applicants ask that the proposed amendments be entered and that all rejections and objections be reconsidered and withdrawn. Enclosed is a check for $60.00 for the extension of time fee. Please apply any other charges or credits to Deposit Account No. 06 1050, referencing Attorney Docket No. 19916-003001.

Respectfully submitted,

Date: September 17, 2007



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